

WHAT IS CLAIMED IS:

1. A composition of matter comprising a vaccinia virus expression vector with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.
2. The composition of claim 1, wherein said composition further comprises an exogenous nucleotide sequence.
3. The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a deletion of nucleic acid sequence.
4. The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus genome from which a thymidine kinase gene is deleted.
5. The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing an insertion of nucleic acid sequence.
6. The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a substitution of nucleic acid sequence.
7. The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a deletion of nucleic acid sequence.
8. The composition of claim 7, wherein said deletion comprises a deletion of the EGF-receptor binding site of said vaccinia virus growth factor gene.
9. The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from a vaccinia virus genome from which at least one vaccinia virus growth factor gene is deleted.
10. The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing an insertion of nucleic acid sequence.

11. The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a substitution of nucleic acid sequence.

12. The composition of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokines, suicide genes, and antigen encoding genes.

13. The composition of claim 12, wherein said tumor suppressor gene is selected from the group consisting of WT1, p53, p16, Rb, and BRCA1.

14. The composition of claim 2; wherein said exogenous nucleotide sequence is selected from the group consisting of cystic fibrosis transmembrane regulator (CFTR), Factor VIII, low density lipoprotein receptor, beta-galactosidase, alpha-galactosidase, beta-glucocerebrosidase, insulin, parathyroid hormone, and alpha-1-antitrypsin.

15. The composition of Claim 1 wherein said vaccinia virus expression vector is produced by a virus particle containing a virus genome, wherein expression of said genome produces a vaccinia virus with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.

16. The composition of Claim 1, wherein said composition present in a mammalian tumor cell.

17. The composition of Claim 1, wherein said vaccinia virus expression vector is VVDD.

18. The composition of Claim 1, wherein said vaccinia virus expression vector is VVDDEGF.

19. A method of introducing an exogenous nucleotide sequence into a mammalian tumor cell in a host, comprising:

providing the composition of Claim 2;

contacting said mammalian tumor cell with said composition; and

expressing said exogenous nucleotide sequence, thereby producing an amount of an expression product.

20. The method of claim 19, wherein said exogenous nucleotide sequence encodes a polypeptide.

21. The method of claim 19, wherein producing said amount of said expression product results in production of an antibody response by said host against said expression product.

22. The method of Claim 19, wherein producing said amount of said expression product results in tumor cell death.

23. A method of using the composition of claim 1, comprising targeting a dividing cell with the composition of claim 1.

24. A method of making the composition of Claim 1, comprising:

providing a vaccinia virus genome;

mutating at least one vaccinia virus growth factor gene of said vaccinia virus genome to produce a negative vaccinia virus growth factor phenotype;

mutating a thymidine kinase gene of said vaccinia virus genome to produce a negative thymidine kinase phenotype; and

introducing an exogenous nucleotide sequence into said vaccinia virus genome, such that a product of said exogenous nucleotide sequence is expressed when said vaccinia virus expression vector is introduced into a target cell.

25. A product made by the method of Claim 24.

26. The method of Claim 24 further comprising the step of combining said composition with a pharmaceutically acceptable carrier.